

CLAIMS

1. A method for the production of cell-specific retroviral vectors comprising the following steps:
- immunizing a mammal with one or more cell population(s),
  - isolating RNA from the immunized mammal, comprising the B cell RNA,
  - production of cDNA regions of the variable regions of the immunoglobulin heavy and light chain from the isolated RNA by means of RT-PCR with primers for the immunoglobulin heavy and light chain wherein the primers comprise the nucleic acid sequence for an oligopeptid linker,
  - ligation of the cDNA regions to scFv-cDNAs,
  - ligation of the scFv-cDNAs into a phagemid-vector and transformation of a host bacterium with the phagemid vector,
  - isolation of phages binding to the cell population(s) used in step a) by means of selection,
  - isolation of cell-specific phages from the phages obtained in step f) which only bind to the cell population(s) used in step a) by means of selection,
  - excision of the scFv-encoding DNA fragments from the cell-specific phages obtained in step g) and ligation into a psi-negative retroviral Env expression vector,
  - transformation of the resulting Env-scFv expression vector into a packaging cell, and
  - isolation of the retroviral vectors secreted by the packaging cell.
2. The method according to claim 1 wherein the cell-specific phages obtained in step g) are isolated.
3. The method according to claim 1 or 2 wherein the steps f) and/or g) are repeated at least once.
4. The method according to ~~any of the claims 1 to 3~~ claim 1 further comprising the step of:  
k) isolating the retroviral vectors secreted by the packaging cell, which transduce the cells of the cell population(s) by means of selection.
5. The method according to ~~any of the claims 1 to 4~~ claim 1 wherein the mammal is selected from the group consisting of mouse, rat, guinea pig, rabbit, goat or sheep.
6. The method according to ~~any of the claims 1 to 4~~ claim 1 wherein the cell population(s) is/are selected from the group consisting of man, mouse, rat, sheep, cattle or pig.

004230.035560

aa

aa

aa

aa

7. The method according to claim 6 wherein the cell population(s) is/are selected from the group comprising T cells, epithelial cells, muscle cells, hematopoietic cells, stem cells, neural cells, carcinoma cells or liver cells.

*a a*  
*Sub. & add B2*  
*aa*  
8. The method according to ~~any of the claims 1 to 7~~ <sup>Claim 1</sup> wherein the env gene of the psi-negative retroviral Env expression vector is derived from spleen necrosis virus (SNV).

9. The method according to claim 8 wherein the expression vector is the vector having the designation pTC53.

10. Retroviral vectors, obtainable by the method according to ~~any of the claims 1 to 9~~ <sup>Claim 1</sup>.

11. The use of the retroviral vectors according to claim 10 as medicament.

12. The use of the vector according to claim 10 for the preparation of a medicament for somatic gene therapy, vaccination therapy or diagnostics.

13. The use of the vector according to claim 10 for the preparation of a medicament for the therapy of cystic fibrosis, ADA deficiency, chronic granulomatosis or HIV-1 infection.

14. Retroviral packaging cell for obtaining the retroviral vectors according to claim 10 transformed with one or more psi-negative expression construct(s) expressing gag, pol and/or env gene products as well as with a psi-negative Env-scFv expression construct according to claim 1h).

15. Retroviral packaging cell according to claim 14 further comprising a psi-positive expression construct comprising a nucleic acid fragment which has to be introduced into the cell to be transduced by the retroviral vector.

16. Retroviral packaging cell according to claim 15 wherein the nucleic acid fragment comprises a therapeutic gene or its DNA fragment and/or a reporter gene or a resistance gene.

17. Retroviral packaging cell according to claim 16 wherein the therapeutic gene or its nucleic acid fragment comprises the CFTR, phox91, ADA, IL-16, p53 or revM10 gene or one or more vaccination gene(s), e.g. recombinant gp120 and IL-16.

004280"0555560

27

18. Retroviral packaging cell according to claim 16, wherein the reporter gene comprises  $\beta$ -galactosidase, "Green Fluorescent Protein", luciferase and the resistance gene neomycin.

004280"03E65560